

Supplement

4

USP XX

NF XV



Contents

People	Officers of the Convention	656
	Board of Trustees	656
	General Committee of Revision	656
	Executive Committee of Revision	657
	Division Executive Committees and Subcommittees ..	658

Admissions
IMPORTANT—Annotated
List of Changes and Additions

New Monographs Appearing in This Supplement	659
General Notices, Monographs, General Chapters, Reagents, and Tables Affected by Changes Appearing in This Supplement	659

Notices	Introduction	666
	USP XX General Notices and Requirements	667
	NF XV General Notices and Requirements	760

Monographs, USP	Official Monographs of USP XX	670
------------------------	-------------------------------------	-----

General	General Tests and Assays	724
	General Information	729

Reagents	Reagents, Indicators, and Solutions	756
-----------------	---	-----

Tables	Description and Relative Solubility of USP and NF Articles	758
	USP and NF Pharmaceutical Ingredients, Listed by Categories	758
	Molecular Formulas and Weights	759

Monographs, NF	Official Monographs of NF XV	761
-----------------------	------------------------------------	-----

Index	Index Cumulative for the Fourth and Preceding Supplements	764
--------------	--	-----

UNITED STATES PHARMACOPEIAL CONVENTION 1980-1985

Officers

FREDERICK E. SHIDEMAN, M.D.,
PH.D.

President
Minneapolis, Minn.

HARRY C. SHIRKEY, M.D.

Vice-President
Highland Heights, Ky.

PAUL F. PARKER, D.Sc.

Treasurer
Lexington, Ky.

JOHN A. OWEN, JR., M.D.

Past President
Charlottesville, Va.

WILLIAM M. HELLER, PH.D.

Secretary
Rockville, Md.

Board of Trustees

WILLIAM J. KINNARD, JR., PH.D.¹

Chairman
Baltimore, Md.

WILLIAM H. BARR, PHARM.D.,

PH.D.¹
Richmond, Va.

JOHN T. FAY, PH.D.²

San Francisco, Calif.

PETER GOLDMAN, M.D.³

(1981-)
Boston, Mass.

FELIX B. GORRELL⁴

(1981-)
Arlington, Va.

ARTHUR HULL HAYES, JR., M.D.³

(1980-1981)
Hershey, Pa.

LEO E. HOLLISTER, M.D.³

Palo Alto, Calif.

IRWIN J. LERNER²

Nutley, N. J.

JOHN A. OWEN, JR., M.D.

ex officio
Charlottesville, Va.

PAUL F. PARKER, D.Sc.

ex officio
Lexington, Ky.

FREDERICK E. SHIDEMAN, M.D.,
PH.D.

ex officio
Minneapolis, Minn.

HARRY C. SHIRKEY, M.D.

ex officio
Highland Heights, Ky.

General Committee of Revision

WILLIAM M. HELLER, PH.D., *Executive Director, USPC*, 12601 Twinbrook Parkway, Rockville, Md. 20852

Chairman, ex officio

LEE T. GRADY, PH.D.⁵

Director, Drug Standards Division

KEITH W. JOHNSON⁵

*Director, Research and
Development, Drug Information
Division*

FAYE G. ABDELLAH

(1981-)
Rockville, Md.

THOMAS J. AMBROSIO, PH.D.

Somerville, N. J.

WILLIAM F. APPEL, B.S.

Minneapolis, Minn.

NORMAN W. ATWATER, PH.D.

Princeton, N. J.

GILBERT S. BANKER, PH.D.

West Lafayette, Ind.

JOHN V. BERGEN, PH.D.

Villanova, Pa.

JOSEPH R. BIANCHINE, PH.D., M.D.

Columbus, Ohio

MARTIN I. BLAKE, PH.D.

Skokie, Ill.

S. GAYLEN BRADLEY, PH.D.

Richmond, Va.

LYNN R. BRADY, PH.D.

Seattle, Wash.

EDWIN D. BRANSOME, JR., M.D.

Augusta, Ga.

WILLIAM H. BRINER, CAPT., B.S.

Durham, N. C.

LARRY C. CAREY, M.D.

Columbus, Ohio

HERBERT S. CARLIN, M.Sc.

Chappaqua, N. Y.

D. MARTIN CARTER, M.D., PH.D.

New York, N. Y.

LESTER CHAFETZ, PH.D.

Morris Plains, N. J.

LESLIE G. CHATTEN, PH.D.

Edmonton, Alberta, Canada

SEBASTIAN G. CIANCIO, D.D.S.

Buffalo, N. Y.

EDWARD F. CLEARY, B.S.

Sandy, Utah

JORDAN L. COHEN, PH.D.

Los Angeles, Calif.

WALTER D. CONWAY, PH.D.

Amherst, N. Y.

¹ Representing pharmacy.

² At large.

³ Representing medicine.

⁴ Public member.

⁵ 12601 Twinbrook Parkway, Rockville, Md. 20852.

- MUFRAV DAVIDSON, M.D.
Jamaica, N. Y.
- LLOYD E. DAVIS, D.V.M., PH.D.
Urbana, Ill.
- JOHN S. DERRYBERRY, M.D.
Shelbyville, Tenn.
- WILLIAM R. EBERT, PH.D.
(1980-1982)
Clearwater, Fla.
- CLYDE R. ERSKINE, B.S., M.B.A.
Philadelphia, Pa.
- DAVID N. F. FAIRBANKS, M.D.
(1981-)
Bethesda, Md.
- EUGENE FARKAS, PH.D.
(1980-1982)
Indianapolis, Ind.
- HARRY W. FISCHER, M.D.
Rochester, N. Y.
- EDWARD A. FITZGERALD, PH.D.
Bethesda, Md.
- KLAUS G. FLOREY, PH.D.
New Brunswick, N. J.
- WILLIAM O. FOYE, PH.D.
Boston, Mass.
- EDWARD D. FROHLICH, M.D.
New Orleans, La.
- SALVATORE A. FUSARI, PH.D.
Morris Plains, N. J.
- JOSEPH F. GALLELLI, PH.D.
Bethesda, Md.
- ALAN GRAY, PH.D.
West Point, Pa.
- MARVIN F. GROSTIC, PH.D.
Kalamazoo, Mich.
- J. KEITH GUILLORY, PH.D.
Iowa City, Iowa
- LOUIS S. HARRIS, PH.D.
Richmond, Va.
- DAVID W. HUGHES, PH.D.
Ottawa, Ontario, Canada
- RODNEY D. ICE, PH.D.,
Oklahoma City, Okla.
- HERBERT E. KAUFMAN, M.D.
New Orleans, La.
- DONALD KAYE, M.D.
Philadelphia, Pa.
- B. J. KENNEDY, M.D.
Minneapolis, Minn.
- LLOYD KENNON, PH.D.
Ocean City, N. J.
- BOEN T. KHO, PH.D.
Rouses Point, N. Y.
- LEWIS J. LEESON, PH.D.
(1982-)
Summit, N. J.
- ROBERT D. LINDEMAN, M.D.
Louisville, Ky.
- MICHAEL D. LOBERG, PH.D.
New Brunswick, N. J.
- JENNIFER LOGGIE, M.B., B.CH.
Cincinnati, Ohio
- WILLIAM J. MADER, M.S.
Sugarloaf Shores, Fla.
- JOHN R. MARKUS, B.S.
Rockville, Md.
- THOMAS MEDWICK, PH.D.
Piscataway, N. J.
- ROSCOE E. MILLER, M.D.
Indianapolis, Ind.
- JOSEPH A. MOLLIKA, PH.D.
Summit, N. J.
- FRED A. MORECOMBE, B.S.
Mesa, Ariz.
- ROBERT F. MORRISSEY, PH.D.
Somerville, N. J.
- JAMES W. MUNSON, PH.D.
Kalamazoo, Mich.
- HAROLD R. NACE, PH.D.
Barrington, R. I.
- WENDEL L. NELSON, PH.D.
Seattle, Wash.
- JOHN L. NEUMEYER, PH.D.
Boston, Mass.
- JENNIFER R. NIEBYL, M.D.
Baltimore, Md.
- STANLEY P. OWEN, PH.D.
Kalamazoo, Mich.
- ROBERT V. PETERSEN, PH.D.
Salt Lake City, Utah
- EDWARD L. PRATT, B.S.
Rensselaer, N. Y.
- JAMES R. RANKIN, B.S.
Taos, N. M.
- BARBARA K. REDMAN, PH.D.
(1980-1981)
Washington, D. C.
- CHRISTOPHER T. RHODES, PH.D.
Kingston, R. I.
- JAY ROBERTS, PH.D.
(1981-)
Philadelphia, Pa.
- JOSEPH R. ROBINSON, PH.D.
Madison, Wis.
- BRUCE C. RUDY, PH.D.
Dallas, Texas
- ANDREW J. SCHMITZ, JR., M.S.
New York, N. Y.
- STEPHEN G. SCHULMAN, PH.D.
Gainesville, Fla.
- MYRON G. SCHULTZ, D.V.M., M.D.
Atlanta, Ga.
- RALPH F. SHANGRAW, PH.D.
Baltimore, Md.
- ALBERT L. SHEFFER, M.D.
Boston, Mass.
- JANE C. SHERIDAN, PH.D.
Nutley, N. J.
- JOSEPH E. SINSHEIMER, PH.D.
Ann Arbor, Mich.
- E. JOHN STABA, PH.D.
Minneapolis, Minn.
- JAMES T. STEWART, PH.D.
Athens, Ga.
- EUGENE A. TIMM, PH.D.
Morristown, N. J.
- MURRAY M. TUCKERMAN, PH.D.
Philadelphia, Pa.
- SAMUEL M. TUTHILL, PH.D.
St. Louis, Mo.
- GERALD W. WALLACE, PH.D.
(1982-)
Indianapolis, Ind.
- WALTER L. WAY, M.D.
San Francisco, Calif.
- ROBERT G. WOLFANGEL, PH.D.
St. Louis, Mo.
- MILTON D. YUDIS, PH.D.
Bloomfield, N. J.
- JOHN E. ZAREMBO, PH.D.
Tuckahoe, N. Y.

Executive Committee of Revision (1982-1983)

WILLIAM H. BRINER, CAPT., B.S.
HERBERT S. CARLIN, M.Sc.
LESTER CHAFETZ, PH.D.

WILLIAM M. HELLER, PH.D., *Chairman*
ROBERT V. PETERSEN, PH.D.

JAMES R. RANKIN, B.S.
ALBERT L. SHEFFER, M.D.

Division Executive Committees and Subcommittees

Drug Standards Division Subcommittees for 1980-1985

WILLIAM M. HELLER, PH.D., *Chairman of the Drug Standards Division Executive Committee*

The Chairmen of the Subcommittees and, ex officio, the Executive Director, constitute the Drug Standards Division Executive Committee.

ANT. Antibiotics

KLAUS G. FLOREY, PH.D., *Chairman*

Lynn R. Brady, Ph.D.; Salvatore A. Fusari, Ph.D.; David W. Hughes, Ph.D.; Donald Kaye, M.D.

B&M. Biochemistry and Microbiology

EUGENE A. TIMM, PH.D., *Chairman*

S. Gaylen Bradley, Ph.D.; Edwin D. Bransome, Jr., M.D.; Edward A. Fitzgerald, Ph.D.; Alan Gray, Ph.D.; Andrew J. Schmitz, Jr.

CH1. Chemistry

LESTER CHAFETZ, PH.D., *Chairman*

William O. Foye, Ph.D.; James W. Munson, Ph.D.; Harold R. Nace, Ph.D.; John L. Neumeyer, Ph.D.; Milton D. Yudis, Ph.D.

CH2. Chemistry

MARTIN I. BLAKE, PH.D., *Chairman*

Walter D. Conway, Ph.D.; Boen T. Kho, Ph.D.; Fred A. Morecombe; Edward L. Pratt; James T. Stewart, Ph.D.; Samuel M. Tuthill, Ph.D.

CH3. Chemistry

NORMAN W. ATWATER, PH.D., *Chairman*

Leslie G. Chatten, Ph.D.; J. Keith Guillory, Ph.D.; Joseph A. Mollica, Ph.D.; Wendel L. Nelson, Ph.D.; Stephen G. Schulman, Ph.D.

CH4. Natural Products

BRUCE C. RUDY, PH.D., *Chairman*

John V. Bergen, Ph.D.; Eugene Farkas, Ph.D. (1980-1982); Joseph E. Sinsheimer, Ph.D.; E. John Staba, Ph.D.; Gerald W. Wallace, Ph.D. (1982-); John E. Zarembo, Ph.D.

C&S. Containers and Stability

THOMAS MEDWICK, PH.D., *Chairman*

Thomas J. Ambrosio, Ph.D.; William F. Appel; John V. Bergen, Ph.D.; Herbert S. Carlin; Clyde R. Erskine

GEN. General Chapters

MURRAY M. TUCKERMAN, PH.D., *Chairman*

Walter D. Conway, Ph.D.; Marvin F. Grostic, Ph.D.; Thomas Medwick, Ph.D.; Fred A. Morecombe; Edward L. Pratt; Samuel M. Tuthill, Ph.D.

M&S. Medical and Surgical Products

STANLEY P. OWEN, PH.D., *Chairman*

Larry C. Carey, M.D.; Edward F. Cleary; Harry W. Fischer, M.D.; Michael D. Loberg, Ph.D.; Robert V. Petersen, Ph.D.

PAR. Parenteral Products

JOSEPH F. GALLELLI, PH.D., *Chairman*

Faye G. Abdellah (1981-); Herbert S. Carlin; Edward F. Cleary; William J. Mader; Robert F. Morrissey, Ph.D.; Barbara K. Redman, Ph.D. (1980-1981); Andrew J. Schmitz, Jr.

PH1. Pharmaceutical Ingredients

RALPH F. SHANGRAW, PH.D., *Chairman*

Gilbert S. Banker, Ph.D.; William R. Ebert, Ph.D. (1980-1982); Lloyd Kennon, Ph.D.; Lewis J. Leeson, Ph.D. (1982-); William J. Mader; Joseph R. Robinson, Ph.D.

PH2. Pharmaceuticals—Dosage Forms and Systems

ROBERT V. PETERSEN, PH.D., *Chairman*

William R. Ebert, Ph.D. (1980-1982); Lloyd Kennon, Ph.D.; Lewis J. Leeson, Ph.D. (1982-); Joseph R. Robinson, Ph.D.

PH3. Pharmaceuticals—Dissolution

JANE C. SHERIDAN, PH.D., *Chairman*

Jordan L. Cohen, Ph.D.; Christopher T. Rhodes, Ph.D.

RAD. Radiopharmaceuticals

WILLIAM H. BRINER, *Chairman*

Rodney D. Ice, Ph.D.; Michael D. Loberg, Ph.D.; Roscoe E. Miller, M.D.; Robert G. Wolfangel, Ph.D.

VET. Veterinary Products

MARVIN F. GROSTIC, PH.D., *Chairman*

Lloyd E. Davis, D.V.M., Ph.D.; Alan Gray, Ph.D.; John R. Markus; Myron G. Schultz, D.V.M., M.D.; Milton D. Yudis, Ph.D.

Drug Information Division Subcommittees for 1980-1985

WILLIAM M. HELLER, PH.D., *Chairman of the Drug Information Division Executive Committee*

Faye G. Abdellah (1981-), William F. Appel, Martin I. Blake, Ph.D., Edwin D. Bransome, Jr., M.D., Herbert S. Carlin, Sebastian G. Ciancio, D.D.S., Lloyd E. Davis, D.V.M., Ph.D., Jennifer Loggie, M.B., B.Ch., James R. Rankin, Barbara K. Redman, Ph.D. (1980-1981), Albert L. Sheffer, M.D., and, ex officio, the Executive Director, constitute the Drug Information Division Executive Committee.

Consumer Interest

JAMES R. RANKIN, *Chairman*

Faye G. Abdellah (1981-); William F. Appel; Sebastian G. Ciancio, D.D.S.; Barbara K. Redman, Ph.D. (1980-1981); Albert L. Sheffer, M.D.

Drug Distribution

HERBERT S. CARLIN, *Chairman*

Faye G. Abdellah (1981-); Thomas J. Ambrosio, Ph.D.; William F. Appel; Sebastian G. Ciancio, D.D.S.; Lloyd E. Davis, D.V.M., Ph.D.; John S. Derryberry, M.D.; Robert V. Petersen, Ph.D.; Barbara K. Redman, Ph.D. (1980-1981)

Therapeutics I

EDWIN D. BRANSOME, JR., M.D., *Chairman*

Murray Davidson, M.D.; John S. Derryberry, M.D.; Harry W. Fischer, M.D.; Louis S. Harris, Ph.D.; Roscoe E. Miller, M.D.; Jennifer R. Niebyl, M.D.

Therapeutics II

ALBERT L. SHEFFER, M.D., *Chairman*

D. Martin Carter, M.D., Ph.D.; Herbert E. Kaufman, M.D.; Donald Kaye, M.D.; Myron G. Schultz, D.V.M., M.D.

Therapeutics III

JENNIFER LOGGIE, M.B., B.Ch., *Chairman*

Joseph R. Bianchine, Ph.D., M.D.; Larry C. Carey, M.D.; Edward D. Frohlich, M.D.; B. J. Kennedy, M.D.; Robert D. Lindeman, M.D.; Walter L. Way, M.D.

Admissions

New Monographs Appearing in This Supplement

USP XX

Acetaminophen and Aspirin Tablets
Acetylcholine Chloride
Acetylcholine Chloride for Ophthalmic Solution
Alumina, Magnesia, and Calcium Carbonate Oral Suspension
Alumina, Magnesia, and Calcium Carbonate Tablets
Amiloride Hydrochloride
Amiloride Hydrochloride Tablets
Amiloride Hydrochloride and Hydrochlorothiazide Tablets
Sterile Ampicillin
Calcium and Magnesium Carbonates Tablets
Calcium Carbonate and Magnesia Tablets
Cefamandole Sodium for Injection
Sterile Cefamandole Sodium
Cephacetrile Sodium
Cephacetrile Sodium for Injection
Chlorzoxazone and Acetaminophen Tablets
Dexpanthenol
Dextrose and Potassium Chloride Injection

Sterile Doxycycline Hyclate
Magnesium Carbonate and Sodium Bicarbonate for Oral Suspension
Manganese Sulfate
Manganese Sulfate Injection
Methenamine Mandelate for Oral Solution
Metronidazole Injection
Sterile Minocycline Hydrochloride
Nystatin for Oral Suspension
Penicillamine Tablets
Chromic Phosphate P 32 Suspension
Tetracycline Hydrochloride Ointment
Sterile Tetracycline Hydrochloride
Sterile Tetracycline Phosphate Complex

NF XV

Polypropylene Glycol

Important—New Changes Adopted Since the Previous Supplement and Addendum and the Fourth Through the Seventh Interim Revision Announcements Were Published Pertain to the Following Titles.

ANNOTATED LIST

General Notices, Monographs, General Chapters, Reagents, and Tables Affected by Changes Appearing in This Supplement

*Page citations refer to the pages of this Supplement.
Note—The absence of a parenthetical term after the section heading denotes a change in the text, as distinguished from a newly added or deleted section.*

General Notices and Requirements (USP XX)

“Official” and “Official Articles,” 667
Abbreviations, 667
Ingredients and Processes, 667
Added Substances, 667
Preservation, Packaging, Storage, and Labeling, 668
Labeling, 668
Expiration Date, 668

Monographs (USP XX)

Acetaminophen Elixir, 670
Packaging and storage
Acetaminophen and Aspirin Tablets (new), 670
Acetylcholine Chloride (new), 670
Acetylcholine Chloride for Ophthalmic Solution (new), 671

Alumina, Magnesia, and Calcium Carbonate Oral Suspension (new), 671
Alumina, Magnesia, and Calcium Carbonate Tablets (new), 672
Amantadine Hydrochloride, 672
Reference standard (added)
Identification
Assay
Amantadine Hydrochloride Capsules, 673
Reference standard (added)
Identification
Assay
Amantadine Hydrochloride Syrup, 673
Reference standard (added)
Identification
Assay
Amibenonium Chloride Tablets, 673
Dissolution (subsections *Medium*, *Apparatus 1*, *Time*, and *Tolerances*)
Amiloride Hydrochloride (new), 673
Amiloride Hydrochloride Tablets (new), 674
Amiloride Hydrochloride and Hydrochlorothiazide Tablets (new), 675
Aminobenzoic Acid, 675
Diazotizable substances (added)

- Aminobenzoic Acid Gel, 675
pH
Alcohol content
Assay
- Aminocaproic Acid Tablets, 676
Dissolution (subsections *pH 9.5 borate buffer*, *Standard preparation*, and *Procedure*)
- Aminophylline Tablets, 676
Disintegration (added)
- Amobarbital Sodium Capsules, 676
Dissolution (added)
- Sterile Ampicillin (new), 676
- Ampicillin for Oral Suspension, 677
Assay (subsections *Assay preparation* and *Procedure*)
- Aspirin Tablets, 677
Disintegration
- Belladonna Tincture, 677
Alcohol content (added)
- Benzoic Acid, 677
Congealing range
- Hydrous Benzoyl Peroxide, 677
Identification
Acidity as benzoic acid (deleted)
Chromatographic purity (added)
Assay
- Benzoyl Peroxide Lotion, 677
Identification
pH (added)
Assay
- Bephenium Hydroxynaphthoate for Oral Suspension, 678
Assay (subsection *Buffer*)
- Sterile Betamethasone Sodium Phosphate and Betamethasone Acetate Suspension, 678
Reference standards
- Bromocriptine Mesylate, 678
Loss on drying
- Brompheniramine Maleate Tablets, 678
Dissolution (subsections *Medium*, *Apparatus*, and *Procedure*)
- Precipitated Calcium Carbonate, 678
Arsenic
- Calcium Carbonate and Magnesia Tablets (new), 678
- Calcium and Magnesium Carbonates Tablets (new), 679
- Calcium Gluceptate Injection, 679
Definition
- Cefaclor for Oral Suspension, 679
pH
- Cefadroxil, 679
Safety
Assay
- Cefadroxil Capsules, 679
Assay
- Cefamandole Nafate, 679
Assay (subsection *Procedure*)
- Cefamandole Sodium for Injection (new), 680
- Sterile Cefamandole Sodium (new), 680
- Cephacetrile Sodium (new), 681
- Cephacetrile Sodium for Injection (new), 681
- Cephalexin, 682
Safety
- Cephaloglycin, 682
Safety
- Cephalothin Sodium for Injection, 682
Reference standard
- Cephradine, 682
Cephalexin content (subsections *Mobile phase* and *pH 8.3 phosphate buffer*)
- Sterile Cephradine, 682
Safety
- Chloramphenicol Capsules, 682
Dissolution (added)
- Chloramphenicol Injection, 683
Assay
- Chloramphenicol, Polymyxin B Sulfate, and Hydrocortisone Acetate Ophthalmic Ointment, 683
Assay for chloramphenicol
- Chlordiazepoxide Hydrochloride Capsules, 683
Content uniformity
- Chlortetracycline Hydrochloride, 683
Reference standard
- Chlortetracycline Hydrochloride Capsules, 683
Reference standard
- Chlortetracycline Hydrochloride Ophthalmic Ointment, 683
Reference standard
- Sterile Chlortetracycline Hydrochloride, 683
Reference standard
- Chlorzoxazone and Acetaminophen Tablets (new), 683
- Clidinium Bromide Capsules, 684
Dissolution (added)
- Clindamycin Phosphate Topical Solution, 684
Assay (subsection *Chromatographic system*, *System suitability*, and *Procedure*)
- Colchicine, 684
Identification
- Sterile Colistimethate Sodium, 684
Definition
Reference standard
Identification (added)
Pyrogen (added)
Safety (added)
Sterility (added)
pH
Loss on drying
Heavy metals
Free colistin (added)
Other requirements
Assay (added)
- Colistin Sulfate, 685
Reference standard
Identification (added)
Safety (added)
pH
Loss on drying
Other requirements (deleted)
Assay (added)
- Colistin Sulfate for Oral Suspension, 685
Definition
Reference standard (added)
pH
Loss on drying
Assay (added)
- Cyclophosphamide Tablets, 685
Disintegration (deleted)
Dissolution (added)
- Cyproheptadine Hydrochloride Tablets, 685
Disintegration (deleted)
Dissolution (added)
- Dactinomycin, 686
Definition
Reference standard
Identification (added)
LD₅₀ (deleted)
Absorptivity (deleted)
Pyrogen (added)
Loss on drying
Crystallinity (added)
Other requirements (deleted)
Assay (added)
- Dactinomycin for Injection, 686
Definition
Reference standard (added)
Identification (added)
LD₅₀ (deleted)
Pyrogen (added)
Sterility (added)
pH
Loss on drying
Other requirements
Assay (added)
- Demeclocycline, 687
Identification (test A)
- Dexamethasone Tablets, 687
Identification
Assay (subsection *Procedure*)
- Dexamethasone Sodium Phosphate, 688
Alcohol
- Dexpanthenol (new), 688

- Dextrose and Potassium Chloride Injection (new), 688
Diazoxide Oral Suspension, 689
 Identification
Dicumarol, 689
 Size of particles (deleted)
Dicumarol Capsules, 689
 Labeling (added)
Dicumarol Tablets, 689
 Labeling (added)
 Disintegration (deleted)
 Dissolution (added)
Digitalis Capsules, 689
 Assay (subsection *Assay preparation*; subheads *Capsules of dry powdered digitalis* and *Capsules of digitalis suspended in water-immiscible media (oil, fat, wax, etc.)*)
Digoxin, 689
 Assay (subsections *Mobile phase*, *Chromatographic system*, *System suitability*, and *Procedure*)
Digoxin Elixir, 690
 Assay (subsections *Mobile phase*, *Chromatographic system* and *System suitability*, and *Procedure*)
Digoxin Injection, 690
 Assay (subsections *Mobile phase*, *Chromatographic system*, and *System suitability*, and *Procedure*)
Digoxin Tablets, 690
 Assay (subsections *Mobile phase*, *Standard preparation*, *Chromatographic system*, and *System suitability*, and *Procedure*)
Diphenhydramine Hydrochloride Capsules, 690
 Dissolution (added)
Diphenoxylate Hydrochloride and Atropine Sulfate Tablets, 690
 Disintegration (deleted)
 Dissolution (added)
Disopyramide Phosphate Capsules, 691
 Dissolution (subsections *Procedure* and *Tolerances*)
Doxepin Hydrochloride, 691
 Assay (subsection *Procedure*)
Doxorubicin Hydrochloride for Injection, 691
 Definition
 Sterility
Doxycycline, 691
 Reference standard
 Identification (added)
 Safety (added)
 pH
 Water
 Crystallinity (added)
 Doxycycline content
 Other requirements (deleted)
 Assay (added)
Doxycycline for Oral Suspension, 692
 Definition
 Reference standard (added)
 Identification (added)
 pH
 Water
 Other requirements (deleted)
 Assay (added)
Doxycycline Calcium Oral Suspension, 692
 Definition
 Reference standard (added)
 Identification (added)
 pH
 Other requirements (deleted)
 Assay (added)
Doxycycline Hyclate, 693
 Definition
 Reference standard
 Identification (added)
 Safety (added)
 pH
 Water
 Crystallinity (added)
 Doxycycline content
 Other requirements (deleted)
 Assay (added)
Doxycycline Hyclate Capsules, 693
 Definition
 Reference standard (added)
 Identification (added)
 Safety (added)
 pH
 Water
 Crystallinity (added)
 Doxycycline content
 Other requirements (deleted)
 Assay (added)
Doxycycline Hyclate for Injection, 694
 Definition
 Reference standard (added)
 Constituted solution (added)
 Identification (added)
 Depressor substances (added)
 Pyrogen (added)
 Safety (added)
 Sterility (added)
 pH
 Loss on drying
 Other requirements (deleted)
 Assay (added)
Sterile Doxycycline Hyclate (new), 694
Doxycycline Hyclate Tablets, 694
 Identification
Doxylamine Succinate Tablets, 695
 Disintegration (deleted)
 Dissolution (added)
Droperidol, 695
 Melting range
Droperidol Injection, 695
 Assay (subsections *Standard preparation* and *Assay preparation*)
Edetate Disodium, 695
 Loss on drying
 Nitrilotriacetic acid (subsection *Standard preparation*)
Emetine Hydrochloride, 695
 Definition
 Loss on drying (deleted)
 Water (added)
Epinephrine, 696
 Specific rotation
Erythromycin Ointment, 696
 Assay
Ethambutol Hydrochloride Tablets, 696
 Dissolution (subsections *Phosphate buffer*, *Bromocresol green solution*, *Standard preparation*, and *Procedure*)
Ethinamate Capsules, 696
 Dissolution (added)
Furazolidone, 696
 Identification (test C)
Furosemide Injection, 696
 Packaging and storage
Gallium Citrate Ga 67 Injection, 696
 Pyrogen
Gelatin, 696
 Arsenic
Gentamicin Sulfate, 697
 Loss on drying
Glutethimide Tablets, 670
 Dissolution (Official date deferred)
Glycerin, 697
 Assay
Green Soap Tincture, 697
 Definition
Hydroxypropyl Methylcellulose 2906, 697
 Assay (subsection *Chromatographic system*)
Hydroxypropyl Methylcellulose Ophthalmic Solution, 698
 Definition
Kanamycin Sulfate, 698
 Chromatographic purity (added)
 Kanamycin B (deleted)
Levorphanol Tartrate, 698
 Specific rotation
Lincomycin Hydrochloride Injection, 698
 Sterility (added)
Magnesium Carbonate and Sodium Bicarbonate for Oral Suspension (new), 698
Magnesium Hydroxide, 699
 Assay
Magnesium Oxide, 699
 Assay

- Magnesium Sulfate, 699
Labeling (deleted)
pH
Manganese Sulfate (new), 699
Manganese Sulfate Injection (new), 699
Mannitol, 699
Melting range
Meperidine Hydrochloride Tablets, 699
Disintegration (deleted)
Dissolution (added)
Methacycline Hydrochloride, 700
Reference standard
Methacycline Hydrochloride Capsules, 700
Reference standard
Water
Assay
Methacycline Hydrochloride Oral Suspension, 700
Reference standard
Assay
Methenamine Tablets, 700
Disintegration (deleted)
Dissolution (added)
Methenamine and Monobasic Sodium Phosphate Tablets, 700
Identification (test C)
Disintegration (deleted)
Dissolution (added)
Methenamine Mandelate for Oral Solution (new), 700
Metoprolol Tartrate Tablets, 701
Reference standard
Assay (subsection *Internal standard solution*)
Metronidazole, 701
Chromatographic purity (added)
Metronidazole Injection (new), 701
Light Mineral Oil, 702
Labeling
Minocycline Hydrochloride, 702
Reference standard
Identification (added)
Safety (added)
pH
Water
Crystallinity (added)
Minocycline content
Other requirements (deleted)
Assay (added)
Minocycline Hydrochloride Capsules, 702
Definition
Reference standard
Weight variation (added)
Water
Assay (added)
Sterile Minocycline Hydrochloride (new), 703
Minocycline Hydrochloride Oral Suspension, 703
Definition
Reference standard (added)
pH
Assay (added)
Minocycline Hydrochloride Tablets, 703
Definition
Weight variation (added)
Water
Assay (added)
Mitomycin for Injection, 703
Safety (added)
Moxalactam Disodium for Injection, 704
Identification
Nitrofurantoin Tablets, 704
Content uniformity
Nystatin, 704
Reference standard
Identification (added)
Safety (added)
pH
Loss on drying
Other requirements (deleted)
Assay (added)
Nystatin-Cream, 704
Definition
Reference standard (added)
Assay (added)
Nystatin Lotion, 704
Definition
Reference standard (added)
pH
Assay (added)
Nystatin Ointment, 705
Definition
Reference standard (added)
Water
Assay (added)
Nystatin Topical Powder, 705
Definition
Reference standard (added)
Loss on drying
Assay (added)
Nystatin Oral Suspension, 705
Definition
Reference standard (added)
pH
Assay (added)
Nystatin for Oral Suspension (new), 705
Nystatin Tablets, 705
Definition
Reference standard (added)
Disintegration
Loss on drying
Assay (added)
Nystatin Vaginal Tablets, 706
Definition
Reference standard (added)
Disintegration
Loss on drying
Assay (added)
Oxazepam Tablets, 706
Disintegration (deleted)
Dissolution (added)
Oxytetracycline, 706
Safety
Sterile Oxytetracycline, 706
Depressor substances
Pyrogen
Oxytetracycline Calcium, 706
Reference standard
Identification (added)
Safety (added)
pH
Water
Calcium content
Crystallinity (added)
Other requirements (deleted)
Assay (added)
Oxytetracycline Calcium Oral Suspension, 707
Definition
Reference standard (added)
Identification (added)
pH
Assay (added)
Oxytetracycline Hydrochloride Capsules, 707
Reference standard (added)
Identification (added)
Weight variation (added)
Loss on drying
Assay (added)
Pectin, 707
Definition
Labeling
Penicillamine, 708
Definition
Reference standard
Identification
Specific rotation
pH
Loss on drying
Residue on ignition
Heavy metals
Penicillin activity
Other requirements (deleted)

- Penicillamine Capsules, 708
 Definition
 Reference standard
 Identification
 Weight variation (deleted)
 Uniformity of dosage units (added)
 Water
 Penicillin activity (deleted)
 Penicillamine Tablets (new), 709
 Penicillin G Benzathine, 709
 Safety
 Sterile Penicillin G Benzathine Suspension, 709
 Definition
 Sterile Penicillin G Procaine with Aluminum Stearate Suspension, 709
 Definition
 Assay
 Sterile Penicillin G Sodium, 709
 Pyrogen
 Phenacetamide Tablets, 709
 Definition
 Phendimetrazine Tartrate, 709
 Chromatographic purity
 Phendimetrazine Tartrate Capsules, 709
 Identification (test A)
 Phenobarbital Sodium, 710
 Assay
 Chromic Phosphate P 32 Suspension (new), 710
 Pilocarpine Ocular System, 710
 Drug release pattern
 Assay
 Sterile Piperacillin Sodium, 711
 Reference standard
 Pyrogen
 Assay (subsections *Standard preparation and Procedure*)
 Sterile Polymyxin B Sulfate, 711
 Assay (subsection *Assay preparation 1*)
 Potassium Permanganate, 711
 Assay
 Propantheline Bromide Tablets, 712
 Disintegration (deleted)
 Dissolution (added)
 Propylene Glycol, 712
 Assay
 Reserpine, 712
 Identification (test B)
 Rifampin, 712
 Absorptivity
 Rolitetracycline for Injection, 712
 Assay
 Bacteriostatic Sodium Chloride Injection, 712
 Labeling
 Sterile Spectinomycin Hydrochloride, 712
 Sterility (added)
 Other requirements
 Stanozolol Tablets, 713
 Disintegration (deleted)
 Dissolution (added)
 Absorbable Surgical Suture, 713
 Definition
 Packaging and storage
 Labeling
 General characteristics (deleted)
 Diameter
 Tensile strength
 Nonabsorbable Surgical Suture, 714
 Definition
 Packaging and storage
 Labeling
 General characteristics (deleted)
 Diameter
 Tensile strength
 Tetracycline, 715
 Reference standard
 Identification (added)
 Absorptivity (deleted)
 Safety (added)
 pH
 Water
 Crystallinity (added)
 4-Epianhydrotetracycline
 Other requirements (deleted)
 Assay (added)
 Tetracycline Oral Suspension, 715
 Definition
 Reference standard (added)
 Identification (added)
 pH
 4-Epianhydrotetracycline
 Assay (added)
 Tetracycline Hydrochloride, 715
 Definition
 Reference standard
 Identification (added)
 Absorptivity (deleted)
 Safety (added)
 pH
 Loss on drying
 Crystallinity (added)
 4-Epianhydrotetracycline
 Other requirements (deleted)
 Assay (added)
 Tetracycline Hydrochloride Capsules, 716
 Definition
 Reference standard (added)
 Identification (added)
 Weight variation (added)
 Loss on drying
 4-Epianhydrotetracycline
 Assay (added)
 Tetracycline Hydrochloride for Injection, 716
 Definition
 Reference standard (added)
 Constituted solution (added)
 Identification (added)
 Pyrogen (added)
 Sterility (added)
 pH
 Loss on drying
 4-Epianhydrotetracycline
 Other requirements
 Assay (added)
 Tetracycline Hydrochloride Ointment (new), 717
 Tetracycline Hydrochloride Ophthalmic Ointment, 717
 Definition
 Reference standard (added)
 Sterility (added)
 Water
 Metal particles (added)
 Other requirements (deleted)
 Assay (added)
 Sterile Tetracycline Hydrochloride (new), 718
 Tetracycline Hydrochloride Ophthalmic Suspension, 718
 Definition
 Reference standard (added)
 Sterility (added)
 Water
 Other requirements (deleted)
 Assay (added)
 Tetracycline Hydrochloride Tablets, 718
 Definition
 Reference standard (added)
 Identification (added)
 Uniformity of dosage units (added)
 Loss on drying
 4-Epianhydrotetracycline content
 Assay (added)
 Tetracycline Phosphate Complex, 719
 Reference standard
 Identification (added)
 Absorptivity (deleted)
 Safety (added)
 pH
 Water
 Chloride (added)
 Crystallinity (added)
 Tetracycline (added)

- 4-Epianhydrotetracycline content
- Other requirements (deleted)
- Assay (added)
- Tetracycline Phosphate Complex Capsules, 719
 - Definition
 - Reference standard (added)
 - Identification (added)
 - Dissolution (added)
 - Uniformity of dosage units (added)
 - Loss on drying
 - 4-Epianhydrotetracycline content
 - Assay (added)
- Tetracycline Phosphate Complex for Injection, 720
 - Definition
 - Reference standard (added)
 - Constituted solution (added)
 - Identification (added)
 - Pyrogen (added)
 - Sterility (added)
 - pH
 - Loss on drying
 - 4-Epianhydrotetracycline content
 - Other requirements
 - Assay (added)
- Sterile Tetracycline Phosphate Complex (new), 721
- Thimerosal Topical Aerosol, 721
 - Definition
- Thimerosal Topical Solution, 721
 - Definition
 - Packaging and storage
- Thimerosal Tincture, 721
 - Definition
 - Packaging and storage
- Thiuridazine, 721
 - Chromatographic purity
- Thiuridazine Hydrochloride, 721
 - Chromatographic purity
- Triamcinolone, 722
 - Assay
- Triamcinolone Acetonide Topical Aerosol, 722
 - Identification
 - Assay (subsections *Standard preparation* and *Assay preparation*)
- Tridihexethyl Chloride Tablets, 722
 - Dissolution (subsection *Apparatus 2*)
- Tyropoate Sodium, 722
 - Iodine and iodide (subsection *Procedure*)
- Vidarabine Concentrate for Injection, 723
 - Definition
- Vinblastine Sulfate, 723
 - Loss on drying
- Vincristine Sulfate, 723
 - Loss on drying
- Bacteriostatic Water for Injection, 723
 - Labeling

General Chapters

General Tests and Assays

GENERAL REQUIREMENTS FOR TESTS AND ASSAYS

- (1) Injections, 724
 - Labeling

MICROBIOLOGICAL TESTS

- (51) Antimicrobial Preservatives—Effectiveness, 724
 - Procedure

CHEMICAL TESTS AND ASSAYS

IDENTIFICATION TESTS

- (181) Identification—Organic Nitrogenous Bases, 724
- (193) Identification—Tetracyclines (new), 725

LIMIT TESTS

- (226) 4-Epianhydrotetracycline (new), 725

PHYSICAL TESTS AND DETERMINATIONS

- (871) Sutures—Needle Attachment, 725
- (881) Tensile Strength, 726
 - (subhead *Surgical Sutures*, subsection *Procedure*; and subhead *Textile Fabrics and Films*, subsection *Procedure*)
- (905) Uniformity of Dosage Units, 726
 - (subhead *Weight Variation* and subhead *Criteria*, subsections *A* and *B*)

General Information

- (1071) Controlled Substances Act Regulations, 729
 - Schedules of Controlled Substances* (Subsections 1308.11, *Schedule I* and 1308.14, *Schedule IV*)
- (1141) Packaging—Child-safety, 752

Reagents, Indicators, and Solutions

REAGENTS

REAGENT SPECIFICATIONS

- Acetanilid (new), 756
- Acetylacetone (new), 756
- Betamethasone (new), 756
- Cadmium Acetate (new), 756
- Carboxymethyl Cellulose (new), 756
- Cellulose, Chromatographic (new), 756
- Cresol, 756
- Fluorene (new), 756
- Isopropylamine, 756
- Nickel-Aluminum Catalyst (new), 756
- n*-Octylamine (new), 756
- Orange IV (new), 756
- Procainamide Hydrochloride (new), 756
- Supports for Gas Chromatography, 756
 - S8 (added)
 - S9 (added)
- Tetraphenylcyclopentadienone (new), 757
- Trifluoroacetic Anhydride (new), 757
- Triphenylstibine (new), 757

SOLUTIONS

TEST SOLUTIONS

- Ammonium Molybdate TS, 757
- Starch TS, 757

REAGENT FOOTNOTES, 757

- 80 (added)
- 81 (added)
- 82 (added)
- 83 (added)

Reference Tables

Description and Relative Solubility of USP and NF Articles, 758

- Acetylcholine Chloride (new)
- Amiloride Hydrochloride (new)
- Butyl Alcohol (new)
- Dexpanthenol (new)
- Ethylnorepinephrine Hydrochloride (new)
- Inulin (new)
- Manganese Sulfate (new)
- Mazindol (new)
- Polypropylene Glycol (new)
- Riboflavin 5'-Phosphate Sodium (new)
- Sulfathiazole (new)
- Tolmetin Sodium (new)

USP and NF Pharmaceutical Ingredients, Listed by Categories,
758*Alcohol Denaturant**Plasticizer*

Mono- and Di-acetylated Monoglycerides

Solvent

Butyl Alcohol

Molecular Formulas and Weights, 759

Acetanilid

Acetylacetone (new)

Amiloride Hydrochloride (new)

Cadmium Acetate (new)

Cefamandole Sodium (new)

Cephacetrile Sodium (new)

Fluorene (new)

n-Octylamine (new)

Trifluoroacetic Anhydride (new)

General Notices and Requirements (NF XV)

“Official” and “Official Articles,” 760

Monographs (NF XV)

Chlorobutanol, 761

*Chloride**Assay*

Croscarmellose Sodium, 761

Degree of substitution

Diethyl Phthalate, 761

Reference standard (added)*Identification*

Ethyl Oleate, 761

Definition

Magnesium Stearate, 761

Identification (test *A*)

Methylene Chloride, 761

Distilling range

Polypropylene Glycol (new), 761

Colloidal Silicon Dioxide, 762

Identification

Sodium Alginate, 762

Starch (deleted)

Sodium Lauryl Sulfate, 762

Sodium sulfate (subsection *Procedure*)

Sodium Starch Glycolate, 762

*Iron**Sodium chloride*

Stearyl Alcohol, 763

*Hydroxyl value**Assay*

Sucrose, 763

Chloride

FOURTH SUPPLEMENT

to USP XX and to NF XV

IMPORTANT—Save the Third Supplement and its Addendum a, published February 15 and June 30, 1982, respectively. This Fourth Supplement is **not cumulative** and does not incorporate the content of previous supplements to USP XX–NF XV, except that it does incorporate the content of all Interim Revision Announcements published since the Third Supplement was issued.

This Fourth Supplement and succeeding supplements will add onto the Third Supplement and its Addendum a; thus, all of these are needed to keep the compendia up to date.

The index of this Supplement is cumulative from 1980, to facilitate reference to all changes and additions to USP XX–NF XV to date.

Introduction

Changes and additions listed herein constitute revisions in USP XX and in NF XV effective May 1, 1983, except where otherwise noted.

This combined USP and NF Supplement is arranged in the order in which the items appear in the USP XX–NF XV main volume.

The Third Supplement comprises pages 1–440 and its Addendum a comprises pages 441–654; this Supplement starts with page 655, and includes an index that pertains to the Third Supplement and its Addendum a and to this Supplement.

The format and general editorial style employed in the Supplement serve not only for printing convenience but also for accommodation to computer storage and retrieval processes.

Explanation of Symbols—

<u>Document</u>	<u>Official Date</u>	<u>Symbols</u>
First Supplement to USP XX and to NF XV	July 1, 1980	■ and ■ ₁
Addendum a to the above	July 1, 1980	▲ and ▲ _{1a}
First Interim Revision Announcement	July 1, 1980	● and ● ₁
Second Supplement	May 1, 1981	■ and ■ ₂
Second Interim Revision Announcement	May 1, 1981	● and ● ₂
Addendum a to Second Supplement	Nov. 1, 1981	▲ and ▲ _{2a}
Third Interim Revision Announcement	Nov. 1, 1981	● and ● ₃
Fourth Interim Revision Announcement	March 1, 1982	● and ● ₄
Third Supplement	May 1, 1982	■ and ■ ₃
Fifth Interim Revision Announcement	May 1, 1982	● and ● ₅
Addendum a to Third Supplement	Sept. 1, 1982	▲ and ▲ _{3a}
Sixth Interim Revision Announcement	Sept. 1, 1982	● and ● ₆
Seventh Interim Revision Announcement	Sept. 1, 1982	● and ● ₇
Fourth Supplement	May 1, 1983	■ and ■ ₄

Superscript symbol denotes the start of a change; *subscript* symbol with numeral or numeral and letter denotes the end of a change.

Where the superscript and subscript symbols appear together with no intervening text, it means that a word or words have simply been deleted.

The figure(s) following a subscript symbol also denote the official date of the change; thus, the numeral "1" refers to the *First* Supplement, and by inference denotes the official date July 1, 1980.

Official Title Changes—NOTE—In all instances where "*Monograph title change (see Note in Introduction)*" is specified, it is to be understood that the official title given after that specification is to be substituted for the former title in the appropriate places throughout the monograph concerned.

In succeeding Supplements, further revisions of the monograph concerned will be shown under the new, currently official title in its respective alphabetic position.

USP XX

General Notices *and* Requirements

"OFFICIAL" AND "OFFICIAL ARTICLES"

Change to read:

The word "official," as used in this Pharmacopeia or with reference hereto, is synonymous with "Pharmacopeial," with "USP," and with "compendial."

The designation USP in conjunction with the official title on the label of an article is a reminder that the article purports to comply with USP standards; such specific designation on the label does not constitute a representation, endorsement, or incorporation by the manufacturer's labeling of the informational material contained in the USP monograph, nor does it constitute assurance by USP that the article is known to comply with USP standards. The standards apply equally to articles bearing the official titles or names derived by transposition of the definitive words of official titles, whether or not the added designation "USP" is used. Names considered to be synonyms of the official titles may not be used for official titles.

Where a product differs from the standards of strength, quality, and purity, ■as determined by the application of the assays and tests, ■₄ set forth for it in the Pharmacopeia, its difference shall be plainly stated on its label. Where a product fails to comply in identity with the identity prescribed in the USP, ■or contains an added substance that interferes with the prescribed assays and tests, ■₄ such product shall be designated by a name that is clearly distinguishing and differentiating from any name recognized in the Pharmacopeia.

Articles listed herein are official and the standards set forth in the monographs apply to them only when the articles are intended or labeled for use as drugs or medical devices and when bought, sold, or dispensed for these purposes.

An article is deemed to be recognized in this Pharmacopeia when a monograph for the article is published in it, including its supplements, addenda, or other interim revisions, and an official date is generally or specifically assigned to it.

The following terminology is used for distinguishing the articles for which monographs are provided: an *official substance* is an active drug entity or a pharmaceutical ingredient or a component of a finished device for which the monograph title includes no indication of the nature of the finished form; a *dosage form* or a *finished device* is the finished, or partially finished (e.g., as in the case of a sterile solid to be constituted into a solution for administration), preparation or product of one or more official substances formulated for use on or for the patient; an *article* is an item for which a monograph is provided, whether an official substance, a dosage form, or a finished device.

ABBREVIATIONS

Change to read:

The expression FDA refers to the U. S. Food and Drug Administration; NBS refers to the National Bureau of Standards. The expression FCC refers to the current edition of the Food Chemicals Codex, including its supplements. The term PhI refers to the International Pharmacopoeia,* published as a recommendation on international standards of strength, quality, and purity for drugs by the World Health Organization. The expressions ACS, ANSI, AOAC, and ASTM refer, respectively, to the American Chemical Society, the American National Standards Institute, the Association of Official Analytical Chemists, and the American Society for Testing and Materials.

■The term RS refers to Reference Standard as stated under *Reference Standards* in the General Notices. ■₄

The terms CS and TS refer to Colorimetric Solution and Test Solution, respectively (see under *Reagents, Indicators, and Solutions*). ■The term VS refers to Volumetric Solution as stated under *Solutions* in the General Notices. ■₄

Abbreviated Statements in Monographs—Incomplete sentences are employed in various portions of the monographs for directness and brevity. Where the limit tests are so abbreviated, it is to be understood that the chapter numbers (shown in angle brackets) designate the respective procedures to be followed, and that the values specified after the colon are the required limits.

INGREDIENTS AND PROCESSES

Change to read:

Added Substances—An official substance, as distinguished from a dosage form, contains no added substances except where specifically permitted in the individual monograph. Where such addition is permitted, the label indicates the name(s) and amount(s) of any added substance(s).

Unless otherwise specified in the individual monograph, or elsewhere in the General Notices, suitable substances such as bases, carriers, coatings, colors, flavors, preservatives, stabilizers, and vehicles may be added to a Pharmacopeial dosage form or finished de-

* With the publication of the Second Edition of the International Pharmacopoeia, *Specifications for the Quality Control of Pharmaceutical Preparations* was shown as its primary title; however, the short title is used also.

vice to enhance its stability, usefulness, or elegance, or to facilitate its preparation. Such substances ■ are regarded as unsuitable and are prohibited unless (a) ■₄ they are harmless in the amounts used, ■(b) ■₄ they do not exceed the minimum quantity required to provide their intended effect, ■(c) ■₄ their presence does not impair the bioavailability or the therapeutic efficacy of the dosage form, and ■(d) ■₄ they do not interfere with the assays and tests prescribed for determining compliance with the Pharmacopeial standards.

Colors—Added substances employed solely to impart color may be incorporated into Pharmacopeial articles that are dosage forms or finished devices, except those intended for parenteral or ophthalmic use, in accordance with the regulations pertaining to the use of colors in drugs issued by the Food and Drug Administration, provided such added substances are otherwise appropriate in all respects. (See also *Added Substances under Injections* (1).)

Capsules and Tablets—Capsules and tablets may be made with suitable diluents, colors, lubricants, disintegrants, and adhesives, such as starches, lactose, sucrose, and other innocuous materials. Tablets and the contents of capsules that are intended to be homogeneous are uniform in appearance within a given lot. Excessive amounts of substances that may impair bioavailability of the active ingredients are to be avoided. Tablets may be coated.

Parenteral and Topical Preparations—For the preservation of preparations intended for parenteral administration or topical application, suitable antioxidants, antimicrobial agents, buffers, and/or stabilizers may be added unless interdicted in the monograph.

For requirements concerning the presence and proportions of added substances in parenteral preparations, and the pertinent labeling requirements, see *Added Substances and Labeling under Injections* (1).

The air in a container of an article for parenteral use may be evacuated or be replaced by carbon dioxide, helium, or nitrogen, or by a mixture of these gases, which fact need not be declared on the label unless otherwise specified in the individual monograph.

Ointments and Suppositories—In the preparation of ointments and suppositories, the proportions of the substances constituting the base may be varied to maintain a suitable consistency under different climatic conditions, provided the concentrations of active ingredients are not varied.

PRESERVATION, PACKAGING, STORAGE, AND LABELING

Change to read:

Labeling—■ The term “labeling” designates all labels and other written, printed, or graphic matter upon an immediate container of an article or upon, or in, any package or wrapper in which it is enclosed, except any outer shipping container. The term “label” designates that part of the labeling upon the immediate container.

A shipping container, unless such container is also essentially the immediate container or the outside of the

consumer package, is exempt from the labeling requirements of this Pharmacopeia.

Articles in this Pharmacopeia are subject to compliance with such labeling requirements as may be promulgated by federal regulations in addition to the Pharmacopeial requirements set forth for the articles.

The potency of some antibiotics, as well as of relatively new drugs generally, is defined in terms of μg or mg of the parent drug (i.e., that portion of the compound which conveys the qualitative pharmacologic activity), even though the antibiotic or other drug used in the dosage form may be in the form of a salt, ester, or other chemical combination. The full name of the chemical combination is used in the content declaration. ■₄

Amount of Ingredient per Dosage Unit—Pharmacopeial articles in capsule, tablet, or other unit dosage form shall be labeled to express the quantity of each therapeutically active ingredient contained in each such unit. Pharmacopeial articles not in unit dosage form shall be labeled to express the quantity of each therapeutically active ingredient in each ml or in each g, or to express the percentage of each such ingredient (see *Percentage Measurements*), except that oral liquids may, alternatively, be labeled in terms of each 5-ml portion.

Labeling Parenteral and Topical Preparations—The label of a preparation intended for parenteral or topical use states the names of all added substances (see *Added Substances*, in these General Notices, and *Labeling under Injections* (1)), and, in the case of parenteral preparations, also their amounts or proportions, except that for substances added for adjustment of pH or to achieve isotonicity, the label may indicate only their presence and the reason for their addition.

Labeling Vitamin-containing Products—The vitamin content of Pharmacopeial preparations shall be stated on the label in metric units. The amounts of vitamins A, D, and E may be stated also in USP Units. Quantities of vitamin A declared in metric units refer to the equivalent amounts of retinol (vitamin A alcohol).

Labeling Electrolytes—The concentration and dosage of electrolytes for replacement therapy (e.g., sodium chloride or potassium chloride) shall be stated on the label in milliequivalents (mEq). The label of the product shall indicate also the quantity of ingredient(s) in terms of weight or percentage concentration.

Special Capsules and Tablets—The label of any form of Capsule or Tablet intended for administration other than by swallowing intact bears a prominent indication of the manner in which it is to be used. Where a tablet is enteric-coated, the label so states.

Change to read:

Expiration Date—The labels of all Pharmacopeial dosage forms ■₁ shall bear an expiration date. The monographs for some dosage forms ■₁ specify the expiration date that shall appear on the label. In the absence of a specific requirement in the individual monograph for a dosage form, ■₁ the label shall bear an expiration date assigned for the particular formu-

lation and package of the article, ■ with the following exception: The label need not show an expiration date in the case of a dosage form packaged in a container that is intended for sale without prescription and the labeling of which states no dosage limitations, and which is stable for not less than 3 years when stored under the prescribed conditions. The expiration■4 date identifies the time during which the article may be expected to meet the requirements of the Pharmacopeial

monograph provided it is kept under the prescribed storage conditions. The expiration date limits the time during which the product may be dispensed or used. Where an expiration date is stated only in terms of the month and the year, it is a representation that the intended expiration date is the last day of the stated month. For articles requiring constitution prior to use, a suitable beyond-use date for the constituted product shall be identified in the labeling.

USP XX Monographs

In the following monograph, the *Dissolution* test is not official at this time. (Via the Seventh Interim Revision Announcement, the *Dissolution* test in this monograph is being held in abeyance until further notice.)

Glutethimide Tablets, page 526 of Addendum *a* to the Third Supplement.

Acetaminophen Elixir

Change to read:

Packaging and storage—Preserve in tight containers. ■■4

Add the following:

■ Acetaminophen and Aspirin Tablets

» Acetaminophen and Aspirin Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$).

Packaging and storage—Preserve in tight containers.

Reference standards—*USP Acetaminophen Reference Standard*—Dry over silica gel for 18 hours before using. *USP Aspirin Reference Standard*—Dry over silica gel for 5 hours before using.

USP Salicylic Acid Reference Standard—Dry over silica gel for 3 hours before using.

Identification—The retention times of the major peaks in the chromatogram of the *Assay preparation* correspond to those of the *Standard preparation*, relative to the internal standard, as obtained in the *Assay*.

Weight variation (931): meet the requirements for *Tablets*.

Salicylic acid—

Solvent mixture, *Mobile phase*, *Internal standard solution*, and *Chromatographic system*—Prepare as directed in the *Assay*.

Procedure—Dissolve a suitable quantity of *USP Salicylic Acid RS*, accurately weighed, in *Solvent mixture* to obtain a solution having a known concentration of about 1.0 mg per ml. Transfer 1.0-ml, 5.0-ml, and 10.0-ml portions, respectively, of this solution to separate 100-ml volumetric flasks, add 10.0 ml of *Internal standard solution* to each flask, dilute with *Solvent mixture* to volume, and mix. Chromatograph these three *Standard solutions* as directed in the *Assay*. Plot the ratios of the peak responses for salicylic acid and benzoic acid for each of the *Standard solutions* versus concentrations, in mg per ml, of salicylic acid, and draw the straight line best fitting the three plotted points. From the graph so obtained, and from the ratio of the peak responses for salicylic acid and benzoic acid in the chromatogram of the *Assay preparation* as obtained in the *Assay*, determine the concentration, in mg per ml, of salicylic acid ($C_7H_6O_3$) in the *Assay preparation*, and calculate the percentage of salicylic acid in relation to the concentration of aspirin in the *Assay preparation*, as determined in the *Assay*. Not more than 3.0% is found.

Assay—[NOTE—Use clean, dry glassware. Inject the *Standard preparation* and the *Assay preparation* promptly after preparation.]

Solvent mixture—Prepare a mixture of chloroform, methanol, and glacial acetic acid (78:20:2).

Mobile phase—Transfer 225 mg of tetramethylammonium hydroxide pentahydrate to a 1000-ml flask, and add 750 ml of water, 125 ml of methanol, 125 ml of acetonitrile, and 1.0 ml of glacial acetic acid. Stir for 3 minutes, filter through a membrane filter (0.3- μ m or finer porosity), and degas.

Internal standard solution—Dissolve benzoic acid in *Solvent mixture* to obtain a solution having a concentration of about 20 mg per ml.

Standard preparation—Transfer about 325 mg of *USP Acetaminophen RS* and about 325 mg of *USP Aspirin RS*, each accurately weighed, to a 100-ml volumetric flask, add 10.0 ml of *Internal standard solution*, dilute with *Solvent mixture* to volume, and mix.

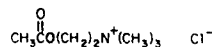
Assay preparation—Weigh and finely powder not less than 20 *Acetaminophen and Aspirin Tablets*. Transfer an accurately weighed portion of the powder, equivalent to about 325 mg of acetaminophen, to a 100-ml volumetric flask, add 10.0 ml of *Internal standard solution* and about 50 ml of *Solvent mixture*, and sonicate for about 3 minutes. Dilute with *Solvent mixture* to volume, and mix. Filter a portion of this solution through a 2.5- μ m or finer porosity filter, and use the filtrate as the *Assay preparation*.

Chromatographic system—The liquid chromatograph is equipped with a 280-nm detector and a 3.9-mm \times 30-cm column that contains packing L1. The flow rate is about 2 ml per minute. Chromatograph four replicate injections of the *Standard preparation*, and record the peak responses as directed under *Procedure*; the relative standard deviation for either analyte is not more than 3.0%.

Procedure—Separately inject equal volumes (about 5 μ l) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The retention times are about 2, 3, 5, and 8 minutes for acetaminophen, salicylic acid (if present), aspirin, and benzoic acid, respectively. Calculate the quantity, in mg, of acetaminophen ($C_8H_9NO_2$) in the portion of *Tablets* taken by the formula $100C(R_U/R_S)$, in which C is the concentration, in mg per ml, of *USP Acetaminophen RS* in the *Standard preparation*, and R_U and R_S are the ratios of the peak responses of acetaminophen and benzoic acid obtained with the *Assay preparation* and the *Standard preparation*, respectively. Calculate the quantity, in mg, of aspirin ($C_9H_8O_4$) in the portion of *Tablets* taken by the same formula, except to read “*USP Aspirin RS*” where “*USP Acetaminophen RS*” is specified, and “aspirin” where “acetaminophen” is specified. ■4

Add the following:

■ Acetylcholine Chloride



$C_7H_{16}ClNO_2$ 181.66

Ethanaminium, 2-(acetyloxy)-*N,N,N*-trimethyl-, chloride. Choline chloride, acetate.

(2-Hydroxyethyl)trimethylammonium chloride, acetate [60-31-1].

» Acetylcholine Chloride contains not less than 98.0 percent and not more than 102.0 percent of $C_7H_{16}ClNO_2$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

Reference standard—*USP Acetylcholine Chloride Reference Standard*—Dry at 105° for 3 hours before using.